What is claimed is:

1. A sustained-release formulation, comprising:

an inner core comprising a therapeutically effective amount of at least one agent, wherein the at least one agent is optionally a free base or a protonated acid, said at least one agent having a solubility in aqueous solution of about 10 mg/ml or less; and

an outer polymer skin covering at least a portion of the inner core.

2. The formulation of claim 1, wherein the inner core further comprises a polymer matrix admixed with the at least one agent.

3. The formulation of claim 1 or 2, wherein the outer polymer skin is polycaprolactone (PCL), poly(vinyl acetate) (PVAC), poly(ethylene-co-vinyl acetate) (EVA), or poly(di-lactide-co-glycolide) (PLGA).

4. The formulation of claim 2, wherein the polymer matrix is polycaprolactone (PCL), poly(vinyl acetate) (PVAC), poly(ethylene-co-vinyl acetate) (EVA), or poly(di-lactide-co-glycolide) (PLGA).

5. The formulation of claim 1 or 2, wherein the outer polymer skin is non-bioerodible.

6. The formulation of claim 5, wherein the non-bioerodible polymer skin is selected from polyurethane, polysilicone, poly(ethylene-co-vinyl acetate), polyvinyl alcohol, and derivatives and copolymers thereof.

7. The formulation of claim 2, wherein the polymer matrix is non-bioerodible.

8. The formulation of claim 7, wherein the non-bioerodible polymer matrix is selected from polyurethane, polysilicone, poly(ethylene-co-vinyl acetate), polyvinyl alcohol, and derivatives and copolymers thereof.

9. The formulation of claim 2, wherein the polymer matrix is bioerodible.

10. The formulation of claim 9, wherein the bioerodible polymer matrix is selected from polyanhydride, polylactic acid, polyglycolic acid, polyorthoester, polyalkylcyanoacrylate, and derivatives and copolymers thereof.

11. The formulation of claim 1 or 2, wherein the outer polymer skin is bioerodible.

12. The formulation of claim 1 or 2, wherein the outer polymer skin is bioerodible and is selected from polyanhydride, polylactic acid, polyglycolic acid, polyorthoester, polyalkylcyanoacrylate, and derivatives and copolymers thereof.

13. The formulation of claim 1 or 2, wherein sustained release of the at least one agent occurs for a period of at least 24 hours and, over that period of release, the concentration of the at least one agent in fluid immediately surrounding the polymer skin is less than 10% of the concentration of the at least one agent in the inner core.

14. The formulation of claim 1 or 2, wherein sustained release of the at least one agent occurs for a period of at least 24 hours and, over that period of release, the concentration of the at least one agent in fluid immediately surrounding the polymer skin is less than 5% of the concentration of the at least one agent in the inner core.

15. The formulation of claim 1 or 2, wherein sustained release of the at least one agent occurs for a period of at least 24 hours and, over that period of release, the concentration of the at least one agent in fluid immediately surrounding the polymer skin is less than 1% of the concentration of the at least one agent in the inner core.

16. The formulation of claim 1 or 2, wherein sustained release of the at least one agent occurs for a period of at least 24 hours and, over that period of release, the concentration of the at least one agent in fluid immediately surrounding the polymer skin is less than 0.1% of the concentration of the at least one agent in the inner core.

17. The formulation of claim 1 or 2, wherein the at least one agent and the outer polymer skin are co-extruded.

18. The formulation of claim 2, wherein the polymer matrix comprises a basic moiety having a pKa higher than the pKa of the at least one agent, or an acidic moiety having a pKa lower than the pKa of the at least one agent.

19. The formulation of claim 1 or 2, wherein the outer polymer skin comprises a basic moiety having a pKa higher than the pKa of the at least one agent, or an acidic moiety having a pKa lower than the pKa of the at least one agent.

20. The formulation of claim 1, wherein the outer polymer skin is impermeable to the at least one agent and covers less than 100% of the inner core.

21. The formulation of claim 1, wherein the outer polymer skin is impermeable to the at least one agent and covers about 75% or less of the inner core.

22. The formulation of claim 1, wherein the outer polymer skin is impermeable to the at least one agent and covers about 50% or less of the inner core.

23. The formulation of claim 1 or 2, wherein the at least one agent in its salt form is selected from timolol maleate, betaxolol hydrochloride, metformin hydrochloride, vancomycin hydrochloride, captopril, erythromycin lactobionate, ranitidine hydrochloride, sertraline hydrochloride, tramadol hydrochloride, ticlopidine hydrochloride, nicotine bitartrate, oxybutynin hydrochloride, diltiazem hydrochloride, propanolol, amoxicillin, cefuroxine axetil, cefaclor, clindamycin, azithromycin, ceftazidine, dorzolamide hydrochloride, acetazolamide, brinzolamide, methazolamide, and dichlorphenamide..

24. A drug delivery device comprising:

a substrate having a surface, and

a sustained-release formulation adhered to the surface, the sustained release formulation comprising an inner core having a therapeutically effective amount of at least one agent, wherein the at least one agent is a free base or a protonated acid, and has solubility

in water that is about 10 mg/ml or less, and an outer polymer skin covering at least a portion of the inner core.

25. The device of claim 24, wherein the inner core further comprises a polymer matrix admixed with the at least one agent.

26. The device of claim 24 or 25, wherein the outer polymer skin is impermeable to the at least one agent and covers less than 100% of the inner core.

27. The device of claim 24 or 25, wherein the outer polymer skin is polycaprolactone (PCL), poly(vinyl acetate) (PVAC), poly(ethylene-co-vinyl acetate) (EVA), or poly(di-lactide-co-glycolide) (PLGA).

28. The device of claim 25, wherein the polymer matrix is polycaprolactone (PCL), poly(vinyl acetate) (PVAC), poly(ethylene-co-vinyl acetate) (EVA), or poly(di-lactide-co-glycolide) (PLGA).

29. The device of claim 24 or 25, wherein the outer polymer skin is non-bioerodible.

30. The device of claim 24 or 25, wherein the outer polymer skin is non-bioerodible and is selected from polyurethane, polysilicone, poly(ethylene-co-vinyl acetate), polyvinyl alcohol, and derivatives and copolymers thereof.

31. The device of claim25, wherein the polymer matrix is non-bioerodible.

32. The device of claim 31, wherein the non-bioerodible polymer matrix is selected from polyurethane, polysilicone, poly(ethylene-co-vinyl acetate), polyvinyl alcohol, and derivatives and copolymers thereof.

33. The device of claim 25, wherein the polymer matrix is bioerodible.

34. The device of claim 33, wherein the bioerodible polymer matrix is selected from polyanhydride, polylactic acid, polyglycolic acid, polyorthoester, polyalkylcyanoacrylate, and derivatives and copolymers thereof.

35. The device of claim 24 or 25, wherein the outer polymer skin is bioerodible.

36. The device of claim 24 or 25, wherein the outer polymer skin is bioerodible and is selected from polyanhydride, polylactic acid, polyglycolic acid, polyorthoester, polyalkylcyanoacrylate, and derivatives and copolymers thereof.

37. The device of claims 24 or 25, wherein sustained release of the at least one agent occurs for a period of at least 24 hours and, over that period of release, the concentration of the at least one agent in fluid outside the polymer skin is less than 10% of the concentration of the at least one agent in the polymer skin.

38. The device of claim 24 or 25, wherein sustained release of the at least one agent occurs for a period of at least 24 hours and, over that period of release, the concentration of the at least one agent in fluid outside the polymer skin is less than 5% of the concentration of the at least one agent in the polymer skin.

39. The device of claim 24 or 25, wherein sustained release of the at least one agent occurs for a period of at least 24 hours and, over that period of release, the concentration of the at least one agent in fluid outside the polymer skin is less than 1% of the concentration of the at least one agent in the polymer skin.

40. The device of claim 24 or 25, wherein the at least one agent and the outer polymer skin are co-extruded.

41. The device of claim 25, wherein the polymer matrix comprises a basic moiety having a pKa higher than the pKa of the at least one agent, or an acidic moiety having a pKa lower than the pKa of the at least one agent.

42. The device of claim 24 or 25, wherein the outer polymer skin comprises a basic moiety having a pKa higher than the pKa of the at least one agent, or an acidic moiety having a pKa lower than the pKa of the at least one agent.

43. The device of claim 24 or 25, wherein the at least one agent in its salt form is selected from timolol maleate, betaxolol hydrochloride, metformin hydrochloride, vancomycin hydrochloride, captopril, erythromycin lactobionate, ranitidine hydrochloride, sertraline hydrochloride, tramadol, ticlopidine hydrochloride, nicotine bitartrate, oxybutynin hydrochloride, diltiazem, propanolol, amoxicillin, cefuroxine axetil, cefaclor, clindamycin, azithromycin, ceftazidine, dorzolamide hydrochloride, acetazolamide, brinzolamide, methazolamide, and dichlorphenamide..

44. A method of providing sustained-release administration of a highly soluble agent, comprising:

providing a therapeutically effective amount of at least one agent, wherein said at least one agent is either a free base or a protonated acid, said at least one agent having a solubility in water that is about 10 mg/ml or less,

forming a sustained-release formulation having an inner core comprising the at least one agent, wherein the inner core is covered at least in part by an outer polymer skin;

providing the sustained-release formulation in a pharmaceutically acceptable carrier; and

administering the sustained-release formulation to a patient.

45. The method of claim 44, wherein the inner core further comprises the at least one agent dispersed in a polymer matrix.

46. The method of claim 44 or 45, wherein the outer polymer skin is impermeable to the at least one agent and covers less than 100% of the inner core.

47. The method of claim 44 or 45, wherein the outer polymer skin is polycaprolactone (PCL), poly(vinyl acetate) (PVAC), poly(ethylene-co-vinyl acetate) (EVA), or poly(di-lactide-co-glycolide) (PLGA).

48. The method of claim 45, wherein the polymer matrix is polycaprolactone (PCL), poly(vinyl acetate) (PVAC), poly(ethylene-co-vinyl acetate) (EVA), or poly(di-lactide-co-glycolide) (PLGA).

49. The method of claim 44 or 45, wherein the outer polymer skin is non-bioerodible.

50. The method of claim 44 or 45, wherein the polymer skin is non-bioerodible and is selected from polyurethane, polysilicone, poly(ethylene-co-vinyl acetate), polyvinyl alcohol, and derivatives and copolymers thereof.

51. The method of claim 45, wherein the polymer matrix is non-bioerodible.

52. The method of claim 51, wherein the non-bioerodible polymer matrix is selected from polyurethane, polysilicone, poly(ethylene-co-vinyl acetate), polyvinyl alcohol, and derivatives and copolymers thereof.

53. The method of claim 45, wherein the polymer matrix is bioerodible.

54. The method of claim 52, wherein the bioerodible polymer matrix is selected from polyanhydride, polylactic acid, polyglycolic acid, polyorthoester, polyalkylcyanoacrylate, and derivatives and copolymers thereof.

55. The method of claim 44 or 45, wherein the outer polymer skin is bioerodible.

56. The method of claim 44 or 45, wherein the outer polymer skin is bioerodible and is selected from polyanhydride, polylactic acid, polyglycolic acid, polyorthoester, polyalkylcyanoacrylate, and derivatives and copolymers thereof.

57. The method of claim 44 or 45, wherein sustained release of the at least one agent occurs for a period of at least 24 hours and, over that period of release, the concentration of the at least one agent in fluid outside the polymer skin is less than 10% of the concentration of the at least one agent in the polymer skin.

58. The method of claim 44 or 45, wherein sustained release of the at least one agent occurs for a period of at least 24 hours and, over that period of release, the concentration of the at least one agent in fluid outside the polymer skin is less than 5% of the concentration of the at least one agent in the polymer skin.

59. The method of claim 44 or 45, wherein sustained release of the at least one agent occurs for a period of at least 24 hours and, over that period of release, the concentration of the at least one agent in fluid outside the polymer skin is less than 1% of the concentration of the at least one agent in the polymer skin.

60. The method of claim 44 or 45, wherein sustained release of the at least one agent occurs for a period of at least 24 hours and, over that period of release, the concentration of the at least one agent in fluid outside the polymer skin is less than 0.1% of the concentration of the at least one agent in the polymer skin.

61. The method of claim 44 or 45, wherein the at least one agent and the outer polymer skin are co-extruded.

62. The method of claim 45, wherein the polymer matrix comprises a base having a pKa higher than the pKa of the at least one agent, or an acidic moiety having a pKa lower than the pKa of the at least one agent.

63. The method of claim 44 or 45, wherein the outer polymer skin comprises a base having a pKa higher than the pKa of the at least one agent, or an acidic moiety having a pKa lower than the pKa of the at least one agent.

64. The device of claim 44 or 45, wherein the at least one agent in its salt form is selected from timolol maleate, betaxolol hydrochloride, metformin hydrochloride, vancomycin hydrochloride, captopril, erythromycin lactobionate, ranitidine hydrochloride, sertraline hydrochloride, tramadol, ticlopidine hydrochloride, nicotine bitartrate, oxybutynin hydrochloride, diltiazem, propanolol, amoxicillin, cefuroxine axetil, cefaclor, clindamycin, azithromycin, ceftazidine, dorzolamide hydrochloride, acetazolamide, brinzolamide, methazolamide, and dichlorphenamide.

65. A method of treating glaucoma comprising:

providing a therapeutically effective amount of a free base of a highly water soluble salt of at least one agent that is effective in the treatment of glaucoma,

forming a sustained-release formulation having an inner core comprising the free base, wherein the inner core is covered at least in part by an outer polymer skin;

providing the sustained release formulation in a pharmaceutically acceptable carrier; and

administering the sustained release formulation to a patient having glaucoma.

66. The method of claim 63, wherein the inner core further comprises the free base dispersed in a polymer matrix.

67. The method of claims 62 or 63, wherein the agent is timolol maleate or betaxolol hydrochloride.